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- ☐ 1. [A new case of acute idiopathic frosted branch angiitis in Europe.](#)  
**V Huerva / T Puig / M C Sánchez / C Jurjo / J Asenjo**, *Eur J Ophthalmol*, Mar 2002  
...to the periphery, **retinal edema** and hemorrhages in...was started on 90 mg  
**prednisolone** daily. After two weeks...absorption of the **retinal edema** and resolution  
of...inflammation. Systemic **prednisolone** were reduced progressively...

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- ☐ 2. [A Case of Frosted Branch Angiitis With Yellowish-White Placoid Lesions - the role of systemic corticosteroids](#)  
**Masuda, K. / Ueno, M. / Watanabe, I.**, *Japanese Journal of Ophthalmology*, Nov 1999  
...Following a decrease in the vascular sheathing and **retinal edema**, systemic  
**prednisolone** was tapered gradually and predniso- lone and prostaglandin...36 in the  
right eye and 2.08 in the left. The **retinal edema** and hemorrhages disappeared but a  
few vascular...

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- ☐ 3. [Air bag-induced corneal flap folds after laser in situ keratomileusis](#)  
**Norden, R.A. / Perry, H.D. / Donnenfeld, E.D. / Montoya, C.**, *American Journal of Ophthalmology*, Aug 2000  
...reaction, and Berlin **retinal edema**. RESULTS: Six weeks...retina showed Berlin  
**retinal edema** of the macula. The...patient was treated with **prednisolone** acetate 1%  
(Pred Forte...the right eye. The **retinal edema** had completely resolved...

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- ☐ 4. [Comparative Ophthalmology Notes: Chapter 2 - Ocular Therapeutics \[57K\]](#)  
Feb 2002  
...Liquifilm® (sulfacetamide and **prednisolone**) - Allergan - suspension. Blephamide

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S.O.P.® (sulfacetamide and **prednisolone**) - Allergan - ointment. Topical...cortisone 0.8, hydrocortisone 1, **prednisolone**/prednisone 4, methylprednisolone...  
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- ☐ 5. [\[A case of presumed radiation optic neuropathy\]](#)  
**O Atsumi / T Sakuraba / S Kimura / K Narita / S Maeda, Nippon Ganka Gakkai Zasshi, May 1991**  
...Funduscopy revealed optic disc swelling with surrounding **retinal edema** and small hemorrhage in the right eye. Fluorescein angiography...large enough to explain the dense central scotoma. Although **prednisolone** therapy gave temporary improvement, the visual function gradually...

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- ☐ 6. [Phacoemulsification and intraocular lens implantation in nanophthalmic eyes - Report of a medium-size series](#)  
**Faucher, A. / Hasanee, K. / Rootman, D.S., Journal of Cataract and Refractive Surgery, May 2002**  
...brimonidine, dorzolamide atropine, **prednisolone** sodium sulfate (Inflammase(R)), ketorolac...ablation of the ciliary body and had some **retinal edema**, accounting for the reduced visual...IOP well controlled at 12 mm Hg on **prednisolone** sodium sulfate every 3 hours and atropine...

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- ☐ 7. [Comparison of tranexamic acid and prednisolone in the treatment of traumatic hyphema - A randomized clinical trial](#)  
**Rahmani, B. / Jahadi, H.R., Ophthalmology, Feb 1999**  
...than did patients receiving **prednisolone** (OR = 1.6 99% CI = 0.6, 4...absorption was the same in TA, **prednisolone**, and placebo groups (4 days...Tranexamic Acid (n = 80) [no. (%)]) **Prednisolone** (n = 78) [no. (%)]) Placebo...subluxation 2 (2) 2 (2) 2 (2) 6 (3) **Retinal edema**/hemorrhage 4 (5) 6 (7) 5...

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Mar 2001  
Proteome mining Bringing in the consultants From the publishers of Pharmacogenomics How gene variants can ruin good drugs March 2001 www.currentdrugdiscovery.com In the year , we introduced Pyrosequencing™, a new technology for applied genomics.  
[http://www.currentdrugdiscovery.com/pdf/2001/3/3comple...]  
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- ☐ 9. [Tuberculin skin testing in uveitis patients and treatment of presumed intraocular tuberculosis in japan<sup>1</sup>](#)  
**Morimura, Y. / Okada, A.A. / Kawahara, S. / Miyamoto, Y. / Kawai, S. / Hirakata, A. / Hida, T., Ophthalmology, May 2002**  
...20/67 Nodule size **Retinal edema** 2 27 F Left 1+ Choroidal...20/20 20/29, 20/20 **Retinal edema** 8 31 F Both 0, 0 Multifocal...20/67 20/20, 20/20 **Retinal edema** 9 36 M Right 0 Multifocal...neovascularization PSL = **prednisolone** RFP = rifampicin VH...

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- ☐ **10. Presumed Choroidal Atypical Tuberculosis Superinfected with Cytomegalovirus Retinitis in an Acquired Immunodeficiency...**  
**Lai, L.-J. / Chen, S.-N. / Kuo, Y.-H. / Ho, J.-D. / Ho, C.-L., Japanese Journal of Ophthalmology, Jul 2002**  
 ...infection. . The left eye revealed moderate vitreous opacity and **retinal edema** (Figure 2) Figure 2 Creamy-white subretinal pigment epithelial...and the vitreous opacity decreased with low dose steroid (**Prednisolone** 10 mg twice a day) treatment for 2 weeks. According to the...  
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- ☐ **11. Primary Anti-Phospholipid Antibody Syndrome (APS) - Current Concepts**  
**Durrani, O.M. / Gordon, C. / Murray, P.I., Survey of Ophthalmology, May 2002**  
 Primary anti-phospholipid syndrome (APS) is a thrombophilic state characterized by recurrent arterial and venous thrombosis, recurrent pregnancy loss, and the presence of circulating anti-phospholipid antibodies that may be responsible...  
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- ☐ **12. Neovascular glaucoma as a complication of retinal vasculitis in Crohn disease**  
**Salmon, J.F. / Ursell, P.G. / Frith, P., American Journal of Ophthalmology, Oct 2000**  
 ...hypertension and was taking 7.5-mg oral **prednisolone** daily. The best-corrected visual acuity...retinal veins, arterial attenuation, **retinal edema**, and scattered cotton-wool spots with...and bendroflurazide. The dose of oral **prednisolone** was increased to 30 mg daily, intensive...  
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- ☐ **13. Medicare Data Utilities Appendices [PDF-980K]**  
 Dec 2002  
 4/97; Prior to 3/94, also included any Liability insurance) E = Workers' compensation F = Public Health Service or other federal agency (other than Dept.  
 [http://hrsonline.isr.umich.edu/rda/userdocs/mdu\_docs/A...]  
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- ☐ **14. Presumed topiramate-induced bilateral acute angle-closure glaucoma**  
**Banta, J.T. / Hoffman, K. / Budenz, D.L. / Ceballos, E. / Greenfield, D.S., American Journal of Ophthalmology, Jul 2001**  
 ...acetazolamide, topical pilocarpine 1% and **prednisolone** acetate 1%, and two doses of intravenous...tartrate 0.2%, timolol maleate 0.5%, and **prednisolone** acetate 1%. A laser peripheral iridotomy...associated with acute glaucoma and **retinal edema** Arch Ophthalmol 80 1968 186 188 3 Jan...  
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- ☐ **15. Ophthalmic Manifestations of Lightning Strike**  
**Norman, M.E. / Albertson, D. / Younge, B.R., Survey of Ophthalmology, Jul 2001**  
 ...Posterior segment Vitreous hemorrhage 49 Retinal detachment 27,49 **Retinal edema** (resembles commotio retinae) 32 Chorioretinal rupture 49...reported previously 50 ), we used a weaning course of topical **prednisolone** acetate drops and cyclopentolate 1%. There is at present...  
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☐ 16. Acute frosted retinal periphlebitis.

**L S Atmaca / K Gündüz**, *Acta Ophthalmol (Copenh)*, Dec 1993

A 30-year-old woman developed bilateral acute vision loss without any systemic symptoms. There was diffuse **retinal edema** and thick perivenous sheathing with moderate vitreous inflammation. Fluorescein angiography showed late staining and dye leakage...

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☐ 17. FLEXIBLE MICROCHIP DEVICES FOR OPHTHALMIC AND OTHER APPLICATIONS

**HERMAN, Stephen, J. / MICROCHIPS, INC.**, *PATENT COOPERATION TREATY APPLICATION*, Jul 2002

Microchip device arrays that can conform to a curved surface are provided for the controlled release or exposure of reservoir contents. The arrays comprise two or more microchip device elements, each of which includes a plurality of reservoirs that...

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☐ 18. [Acute generalized retinal periphlebitis (author's transl)]

**H Bleckmann / G Norderhus**, *Klin Monatsbl Augenheilkd*, Jul 1980

Report on a 28-year-old man with acute impairment of vision (blurring) who was subsequently found to have extensive bilateral **retinal edema** with hemorrhages at posterior pole. A striking feature was the periphlebitic sheathing in this area. After systemic corticosteroid...

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☐ 19. A case of frosted-branch retinal angiitis in a child.

**A Nakai / S Saika**, *Ann Ophthalmol*, Nov 1992

...frosted-branch angiitis of the retina in a 3-year-old girl. She had acute visual disturbances OU, and we observed iritis, **retinal edema**, and retinal angiitis. Retinal angiitis showed the same condition as previously described, the so-called acute frosted retinal...

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☐ 20. Analysis of 87 Cases with Vogt-Koyanagi-Harada Disease

**Mondkar, S.V. / Biswas, J. / Ganesh, S.K.**, *Japanese Journal of Ophthalmology*, May 2000

...detachment in 44 (50.6%) cases, **retinal edema** in 25 (28.7%) cases. The...body weight) in the form of **prednisolone** tablets. We adopted a single...cases (56.3%). Following oral **prednisolone** therapy, 61.6% showed improvement...common finding and marked **retinal edema** with disc edema was also...

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☐ 21. Uveitis in nephrotic syndrome.

**M Iwasaki / Y Kusumoto / T Amemiya**, *Metab Pediatr Syst Ophthalmol*, Feb 1993

...She had many cells in the anterior chamber, fine granular keratitic precipitates on the posterior surface of the cornea and **retinal edema** around the optic disc. Diabetes mellitus had been diagnosed, but it was considered to be steroid diabetes mellitus. This...

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- ☐ 22. [Retinal vasculitis occurring with common variable immunodeficiency syndrome](#)  
**van Meurs, J.C. / Lightman, S. / de Waard, P.W.T. / Baarsma, G.S. / van Suijlekom-Smit, L.W.A. / van de Merwe, J.P. / de Groot, R.,** *American Journal of Ophthalmology*, Feb 2000  
 ...Bilateral retinal vasculitis and diffuse **retinal edema** were present in all three patients...retinal vasculitis with widespread **retinal edema** and diffuse capillary leakage, two...increasing doses of oral and intravenous **prednisolone** to no avail, but the addition of cyclosporin...

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- ☐ 23. [Retinal vasculitis: a diagnostic dilemma](#)  
**Bisighini, S.L. / Pagliuso, L.M.,** *Clinical Eye and Vision Care*, Jun 1997  
 ...secondary changes: Vascular occlusion Retinal infarction **Retinal edema** Macular edema Optic nerve edema Attenuated vessels Optic...include retinal hemorrhages, cotton wool spots, hard exudate, **retinal edema** and retinal neovascularization. Al- though this microvasculopathy...

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- ☐ 24. [\[A 50-year-old man with metamorphopsia and optic nerve swelling\]](#)  
**Y Nakajima / T Kitada / Y Mizutani / Y Yamamoto / N Kuwabara / T Sato / T Kondo / Y Mizuno,** *No To Shinkei*, May 1993  
 ...metamorphopsia associated with **retinal edema**. He was well until one month...abnormalities were bilateral papilledema, **retinal edema** and horizontal nystagmus with...methotrexate, cytarabine and **prednisolone** were administered. He was also...

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- ☐ 25. [Ocular and systemic manifestations of the acquired connective tissue diseases: Part I](#)  
**Atkin, S.R.,** *Clinical Eye and Vision Care*, Jun 1996  
 The connective tissue diseases are musculoskeletal disorders which have multisystemic involvement, frequently have associated ocular manifestations, and although the specific etiologies are unknown, they all demonstrate abnormalities of...

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- ☐ 26. [Two neuro-ophthalmic episodes separated in time and space](#)  
**Cullom, R.D. / Cullom, M.E.,** *Survey of Ophthalmology*, Nov 1995  
 ...She saw her ophthalmologist who prescribed sulfacetamide/**prednisolone** solution OD. Five days later she was seen by her ophthalmologist...When a patient presents with acute monocular visual loss and **retinal edema**, attention should be focused on two major questions: 1) What...

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- ☐ **27. Retinal artery occlusion**  
**Mangat, H.S.,** *Survey of Ophthalmology*, Sep 1995  
 ...with good visual acuity (20/40 average). They have visual field abnormalities that correspond to the distribution of the **retinal edema** and infarction and these defects usually remain permanently. If artery-to-artery collateral vessels develop they are almost...  
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- ☐ **28. The treatment of rheumatoid arthritis**  
**Wright, V.,** *Journal of Chronic Diseases*, Jan 1963  
 And of these disorders rheumatoid arthritis occupies a most prominent place because of its prevalence, its incidence at all ages, and the crippling deformities it often produces.  
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- ☐ **29. Ocular coccidioidomycosis**  
**Rodenbiker, H.T. / Ganley, J.P.,** *Survey of Ophthalmology*, Mar 1980  
 Coccidioidomycosis has been recognized as a common systemic disease since the late 1930's. The occurrence of ocular lesions associated with the systemic infection is uncommon. The anterior segment manifestations appear to be a mild...  
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- ☐ **30. Developmental implications of ocular pharmacology**  
**Kahan, A.,** *Pharmacology and Therapeutics*, Jan 1985  
 Pharmac. Ther, Vol. 28, pp. 163 to 226, 1985 0163-7258/85 \$0,00 + 0.50 Printed in Great Britain. All rights reserved Copyright {Z; 1985 Pergamon Press Ltd Specialist Subject Editor: J. GY.  
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- ☐ **31. Paroxysmal hypertension in aortitis syndrome**  
**Tanaka, N. / Tanaka, H. / Toyama, Y. / Kashima, T. / Niimura, T. / Kanehisa, T.,** *American Heart Journal*, Sep 1975  
 ...Slight bilateral choked discs and **retinal edema** and folds in the nasal side of the...evident (Table 1). Oral administration of **prednisolone** started at the tenth hospital day brought...observed in A and C, but not in B. with **prednisolone** reliably controlled both the severity...  
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- ☐ **32. Fluids in the anterior part of the optic nerve in health and disease**  
**Hayreh, S.S.,** *Survey of Ophthalmology*, Jul 1978  
 New techniques have recently made it possible to study the flow of fluids (blood, axoplasm, and interstitial fluid) in the anterior part of the optic nerve. Blood flow has been reviewed previously; axoplasm and interstitial fluid are...  
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- ☐ **33. A survey of Allergy's present position - Classification of clinical and pathologic features of allergic disorders**

**Hartman, M.M.**, *The American Journal of Medicine*, Jul 1956

...Canker sores8 Exacerbations of gout50'63 Sudden death in the hyperrcactor state114  
Erythema multiforme7 Retinal detachment'1 ' **Retinal edema** and hemorrhage111  
Uveitis24'111 Reiter's disease70'72 Loeffler's syndrome6 Temporal arteritis29'47  
Ulcerative colitis2 Regional...

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☐ **34. [Neurologic involvement in seven patients with Behcet's disease](#)**

**O'Duffy, J.D. / Goldstein, N.P.**, *The American Journal of Medicine*, Aug 1976

...Case Treatment Daily Dose (mg) Outcome 1 2 34 5 Prednisone Cyclophosphamide  
Prednisone Azathioprine Prednisone Azathioprine **Prednisolone** None 40-60 150-200 60-  
5 150-50 15-30 150-50 32-16 Died Good suppression Partial suppressionPartial  
suppression Died, myocardial...

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☐ 1. [Diabetic Retinopathy - More Than Meets the Eye](#)

**Gardner, T.W. / Antonetti, D.A. / Barber, A.J. / LaNoue, K.F. / Levison, S.W. / The Penn State Retina Research Group, *Survey of Ophthalmology*, Dec 2002**

...are affected long before the onset of clinically evident **nonproliferative** retinopathy. They paradoxically express more GFAP in contrast...macular edema. Histologic examination of a retina with **nonproliferative** diabetic retinopathy shows that in addition to cystoid...

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☐ 2. [COMPOUNDS AND METHOD FOR THE PREVENTION AND TREATMENT OF DIABETIC RETINOPATHY](#)

**BODOR, Nicholas, Stephen / GRANT, Maria, Bartolomeo / UNIVERSITY OF FLORIDA, *PATENT COOPERATION TREATY APPLICATION*, Mar 1999**

The invention provides peptide derivatives designed to deliver peptides having growth factor inhibitory activity, especially somatostatin analogs, to the retina by sequential metabolism. The peptide derivatives, which comprise a dihydropyridine &iff;...

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May 2002  
...McCluskey Steroids Intravitreal triamcinolone R. Danis **Anecortave** acetate M.D. de Smet Steroid implants B. Kuppermann Video...Neurotrophic factor signalling in retinal photoreceptors D. Hicks **Glucocorticoids** directly increase retinal endothelial cell barrier properties...  
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Jul 2001  
...satisfactory drug therapies. **Anecortave** acetate (AL-3789) is a new...models of neovascularization. **Anecortave** acetate is devoid of conventional...the ocular liability of a **glucocorticoid**. Preclinical toxicology and...clinical studies show that **anecortave** acetate is a safe angiostatic...  
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May 2002  
...induced indirectly by **glucocorticoids** in TM cells. Glaucomatous...Y O C is involved in **glucocorticoid**- induced ocular hypertension...discovered a new agent, **anecortave** acetate, which suppresses the **glucocorticoid** induction of M Y O C...  
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- ☐ 4. REDUCTION OR PREVENTION OF PDT RELATED INFLAMMATION  
**LEVY, Julia, G. / QLT INC., PATENT COOPERATION TREATY APPLICATION**, Aug 2002  
This invention relates generally to the field of pharmacotherapeutics and the use of photodynamic therapy ("PDT"). In particular, the invention provides a method for reducing or preventing the effects of inflammation arising from normal dose...  
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Jul 2001  
...satisfactory drug therapies. **Anecortave** acetate (AL- 3789) is a new...models of neovascularization. **Anecortave** acetate is devoid of conventional...the ocular liability of a **glucocorticoid**. Preclinical toxicology and...clinical studies show that **anecortave** acetate is a safe angiostatic...  
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- ☐ 6. RETINAL DISEASE AND GLAUCOMA - New Therapeutic Strategies [27K]  
Mar 2002  
...induced indirectly by **glucocorticoids** in TM cells. Glaucomatous...MYOC is involved in **glucocorticoid**-induced ocular hypertension...discovered a new agent, **anecortave** acetate, which suppresses the **glucocorticoid** induction of MYOC in...  
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...induced indirectly by **glucocorticoids** in TM cells. Glaucomatous...Y O C is involved in **glucocorticoid**- induced ocular hypertension...discovered a new agent, **anecortave** acetate, which suppresses the **glucocorticoid** induction of M Y O C...  
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Cost is in DialUnits		
?		
Terminal set to DLINK		
? b 5,34,71,155		
19may06 16:57:31 User291213 Session D21.1		
	\$0.39	0.112 DialUnits File1
\$0.39		Estimated cost File1
\$0.10		TELNET
\$0.49		Estimated cost this search
\$0.49		Estimated total session cost 0.112 DialUnits

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	136	ANECORTAVE
	177	PREGNADIEN
S1	311	ANECORTAVE OR PREGNADIEN
? s	nonproliferative or	retinopathy or edema
	2179	NONPROLIFERATIVE
	62455	RETINOPATHY
	184888	EDEMA
S2	245075	NONPROLIFERATIVE OR RETINOPATHY OR EDEMA
? s	s1 and s2	
	311	S1
	245075	S2
S3	19	S1 AND S2
? rd		
S4	12	RD (unique items)
? s	s4 and py<2003	
Processing		
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	41670827	PY<2003
S5	3	S4 AND PY<2003
? t	s5/full/all	

5/9/1 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0012906237 BIOSIS NO.: 200100078076

**The effect of an angiostatic steroid on neovascularization in a rat model of retinopathy of prematurity**

AUTHOR: Penn John S (Reprint); Rajaratnam Veeraramani S; Collier Robert J; Clark Abbot F

AUTHOR ADDRESS: Department of Ophthalmology and Visual Sciences, Vanderbilt University School of Medicine, 2115 21st Avenue South, 8016 Medical Center East, Nashville, TN, 37232-8808, USA\*\*USA

JOURNAL: IOVS 42 (1): p283-290 January, 2001 2001

MEDIUM: print

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

**ABSTRACT:** Purpose. The inhibition of angiogenesis by angiostatic steroids has been demonstrated in a variety of systems, including rabbit and rat cornea. There is considerable interest in the therapeutic potential of this class of compounds for angiogenic ocular conditions such as diabetic **retinopathy**, macular degeneration, and **retinopathy** of prematurity (ROP). This study was designed to test the capacity of an angiostatic steroid, **anecortave** acetate, to inhibit retinal neovascularization using a rat model of ROP and to investigate the mechanism of the effect. Methods. At birth, rats were placed in an atmosphere of varying oxygen that produces retinal neovascular changes that approximate human ROP. The rats then received intravitreal injections of either **anecortave** acetate or vehicle at varying times, and all were subsequently placed in room air. Retinas were assessed for plasminogen activator inhibitor (PAI)-1 mRNA level by RNase protection assay at 1, 2, and 3 days after injection and for normal and abnormal blood vessel growth 3 days later. Results. A significant reduction in the severity of abnormal retinal neovascularization was observed in the steroid-treated eyes compared with vehicle-injected eyes in ROP rats, yet the extent of normal total retinal vascular area was not significantly different. The drug had no effect on either retinal vascular area or neovascularization when tested in room air-raised control rats. Drug-injected eyes demonstrated a six- to ninefold increase in PAI-1 mRNA at 1 to 3 days after injection. Conclusions. This study represents the first therapeutic effect of an angiostatic steroid in an animal model of neovascular **retinopathy**. Additionally, the induction of PAI-1 indicates a mechanism of action for this class of compounds, and this is a novel finding in vivo. Because **anecortave** acetate significantly inhibited pathologic retinal angiogenesis in this model, while not significantly affecting normal intraretinal vessels, it holds therapeutic potential for a number of human ocular conditions in which angiogenesis plays a critical pathologic role.

REGISTRY NUMBERS: 7753-60-8: **anecortave** acetate

**DESCRIPTORS:**

MAJOR CONCEPTS: Pharmacology; Sense Organs--Sensory Reception

BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: rat (Muridae)--animal model, strain-Sprague-Dawley

ORGANISMS: PARTS ETC: retina--sensory system

COMMON TAXONOMIC TERMS: Animals; Chordates; Mammals; Nonhuman Vertebrates; Nonhuman Mammals; Rodents; Vertebrates

DISEASES: **retinopathy** of prematurity--eye disease, treatment

MESH TERMS: **Retinopathy** of Prematurity (MeSH)

CHEMICALS & BIOCHEMICALS: **anecortave** acetate {4,9(11)- **pregnadien** -17-alpha,21-diol-3,20-dione-21-acetate)--ophthalmic-drug, angiostatic

steroid, structure, usefulness; plasminogen activator inhibitor-1  
messenger RNA--induction

METHODS & EQUIPMENT: RNase protection assay--analytical method

MISCELLANEOUS TERMS: retinal neovascularization--inhibition

CONCEPT CODES:

22031 Pharmacology - Sense organs, associated structures and functions

10062 Biochemistry studies - Nucleic acids, purines and pyrimidines

12512 Pathology - Therapy

20004 Sense organs - Physiology and biochemistry

20006 Sense organs - Pathology

22002 Pharmacology - General

BIOSYSTEMATIC CODES:

86375 Muridae

5/9/2 (Item 2 from file: 5)

DIALOG(R) File 5:Biosis Previews(R)

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0012456150 BIOSIS NO.: 200000174463

New steroidal anti-inflammatory antedrugs: Methyl

21-desoxy-21-chloro-11beta,17alpha-dihydroxy-3,20-dioxo-1,4-pregnadiene-1

6alpha-carboxylate, methyl

21-desoxy-21-chloro-11beta-hydroxy-3,20-dioxo-1,4-pregnadiene-16alpha-carboxylate, and their 9alpha-fluoro derivatives

AUTHOR: Ko Dong-Hoon; Heiman Ann S; Chen Meiqin; Lee Henry J (Reprint)

AUTHOR ADDRESS: Center for Anti-inflammatory Research, College of Pharmacy  
and Pharmaceutical Sciences, Florida A and M University, Tallahassee, FL,  
32307-3800, USA\*\*USA

JOURNAL: Steroids 65 (4): p210-218 April, 2000 2000

MEDIUM: print

ISSN: 0039-128X

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: To a series of 21-desoxy-21-chloro-corticosteroids, a metabolically labile methoxycarbonyl group at C-16 has been incorporated. The approach is to synthesize locally active compounds that are hydrolyzed to inactive and readily excretable acid metabolites upon entry into the systemic circulation. Novel antedrugs were evaluated for anti-inflammatory activity and their adverse effects in an acute and semichronic croton oil-induced ear **edema** bioassay. Binding affinity to glucocorticoid receptors and induction of L-tyrosine-2-oxoglutarate aminotransferase were studied in hepatoma tissue culture cells. After a single topical application in the croton oil-induced ear **edema** bioassay, treatment with all the compounds resulted in dose-dependent inhibition of **edema**. From these dose-response profiles, the following ID50 values (nmol/ear resulting in a 50% reduction of **edema**) were calculated: 540, 618, 454, and 346 nmol for prednisolone (P), methyl 21-desoxy-21-chloro-11beta,17alpha-dihydroxy-3,20-dioxo-1,4- **pregnadien** -16alpha-carboxylate (PClCM), methyl 21-desoxy-21-chloro-11beta,17alpha-dihydroxy-9alpha-fluoro-3,20-dioxo-1,4- **pregnadien** -16alpha-carboxylate (FPClCM), and methyl 21-desoxy-21-chloro-9alpha-fluoro-11beta-hydroxy-3,20-dioxo-1,4- **pregnadien** -16alpha-carboxylate (FDPClCM), respectively. Results of the 5-day rat croton oil ear **edema** bioassay indicated that, in contrast with the parent compound P, the novel steroidal antedrugs did not significantly alter body weight gain, thymus weights, or plasma corticosterone levels. The binding affinities for cytosolic hepatoma

tissue culture glucocorticoid receptors were 33, 201, 471, 5304, and 3765 nM for P, PClCM, FPClCM, methyl 21-desoxy-21-chloro-11beta-hydroxy-3,20-dioxo-1,4- **pregnadien** -16alpha-carboxylate (D PClCM), and FDPClCM, respectively. Collectively, results of these investigations suggest that modifications of P, which included replacement of 21-hydroxyl group with chlorine and addition of 16-methoxycarbonyl group with or without 17-hydroxyl moiety, retained the topical anti-inflammatory activity of the parent compound P without significant adverse systemic effects.

REGISTRY NUMBERS: 9014-55-5: L-tyrosine-2-oxoglutarate aminotransferase;  
50-22-6: corticosterone

DESCRIPTORS:

MAJOR CONCEPTS: Pharmacology

BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: rat (Muridae)

COMMON TAXONOMIC TERMS: Animals; Chordates; Mammals; Nonhuman Vertebrates ; Nonhuman Mammals; Rodents; Vertebrates

DISEASES: hepatoma--digestive system disease, neoplastic disease

MESH TERMS: Carcinoma, Hepatocellular (MeSH); Liver Neoplasms (MeSH)

CHEMICALS & BIOCHEMICALS: 9 alpha-fluor derivatives--

antiinflammatory-drug; FPClCM--antiinflammatory-drug, side effects;

L-tyrosine-2-oxoglutarate aminotransferase; PClCM--

antiinflammatory-drug, side effects; corticosterone--plasma;

glucocorticoid receptors

MISCELLANEOUS TERMS: body weight; **edema** ; thymus weight

CONCEPT CODES:

22002 Pharmacology - General

12002 Physiology - General

24002 Neoplasms - General

14001 Digestive system - General and methods

BIOSYSTEMATIC CODES:

86375 Muridae

5/9/3 (Item 3 from file: 5)

DIALOG(R) File 5:Biosis Previews(R)

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0006071740 BIOSIS NO.: 198885040631

**SYNTHESIS OF NEW ANTIINFLAMMATORY STEROIDAL 20 CARBOXAMIDES 20R AND 20S-21-N-SUBSTITUTED AMINO-11-BETA 17 20-TRIHYDROXY-3 21-DIOXO-1 4-PREGNADIENE**

AUTHOR: KIM H P (Reprint); BIRD J; HEIMAN A S; HUDSON G F; TARAPOREWALA I B ; LEE H J

AUTHOR ADDRESS: CENT ANTI-INFLAMMATORY RES, COLL PHARM, FLA A AND M UNIV, TALLAHASSEE, FLA 32307, USA\*\*USA

JOURNAL: Journal of Medicinal Chemistry 30 (12): p2239-2244 1987

ISSN: 0022-2623

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: The synthesis and antiinflammatory activities of new steroidal 20-carboxamides, (20R)- and (20S)-21-(N-substituted amino)-11.beta.,17,20-trihydroxy-3,21-dioxo-1,4-pregnadiene (5-8) are described. These compounds were prepared from the respective isomer of 20-dihydroprednisolonic acid, (20R)- and (20S)-11.beta.,17,20-trihydroxy-3-oxo-1,4- **pregnadien** -21-oic acid (4a and 4b), by coupling with primary amines after the activation of the

steroid acid with N,N1-dicyclohexylcarbodiimide (DDC) and 1-hydroxybenzotriazole. Confirmation of the configurational assignment at C-20 of the 20-carboxamides was achieved by reduction of methyl (20R)- and (20S)-11.beta.,17,20-trihydroxy-3-oxo-1,4- **pregnadien** -21-oate (3a and 3b) to the known stereochemistry at C-20 of (20R)- and (20S)-11.beta.,17,20,21-tetrahydroxy-3-oxo-1,4-pregnadiene (2a and 2b). The topical antiinflammatory activities of these steroidal 20-carboxamides were assessed by the croton oil induced ear **edema** assay in rats and their local and systemic antiinflammatory activities by the cotton pellet granuloma bioassay. Results of these investigations suggest a structure-activity relationship where carboxamide derivatives with the 20(R)-hydroxy configurations exhibit higher potency than those with the 20-(S)-hydroxy configurations. The amides of steroidal 21-oic acids with high local antiinflammatory potency exhibited systemic activities unlike the corresponding esters of steroidal 21-oic acids, which are devoid of systemic activities.

DESCRIPTORS: RAT ANTIINFLAMMATORY-DRUG

DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Endocrine System-- Chemical Coordination and Homeostasis; Pathology; Pharmacology

BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia

COMMON TAXONOMIC TERMS: Animals; Chordates; Mammals; Nonhuman Vertebrates ; Nonhuman Mammals; Rodents; Vertebrates

CONCEPT CODES:

10057 Biochemistry methods - Sterols and steroids  
 10066 Biochemistry studies - Lipids  
 10067 Biochemistry studies - Sterols and steroids  
 10506 Biophysics - Molecular properties and macromolecules  
 12508 Pathology - Inflammation and inflammatory disease  
 17004 Endocrine - Adrenals  
 22012 Pharmacology - Connective tissue, bone and collagen-acting drugs  
 22016 Pharmacology - Endocrine  
 22501 Toxicology - General and methods  
 51522 Plant physiology - Chemical constituents

BIOSYSTEMATIC CODES:

86375 Muridae

? ds

Set	Items	Description
S1	311	ANECORTAVE OR PREGNADIEN
S2	245075	NONPROLIFERATIVE OR RETINOPATHY OR EDEMA
S3	19	S1 AND S2
S4	12	RD (unique items)
S5	3	S4 AND PY<2003

? logoff

19may06 17:00:19 User291213 Session D21.2

\$5.93 1.005 DialUnits File5  
 \$6.15 3 Type(s) in Format 9  
 \$6.15 3 Types

\$12.08 Estimated cost File5  
 \$17.11 0.729 DialUnits File34  
 \$17.11 Estimated cost File34  
 \$1.29 0.146 DialUnits File71  
 \$1.29 Estimated cost File71  
 \$3.33 0.979 DialUnits File155  
 \$3.33 Estimated cost File155  
 OneSearch, 4 files, 2.859 DialUnits FileOS  
 \$0.80 TELNET  
 \$34.61 Estimated cost this search

\$35.10 Estimated total session cost 2.972 DialUnits

Logoff: level 05.11.05 D 17:00:19

You are now logged off



Welcome to DIALOG

Dialog level 05.11.05D

Last logoff: 18may06 15:50:07

Logon file001 19may06 10:39:22

\*\*\* ANNOUNCEMENTS \*\*\*

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NEW FILES RELEASED

\*\*\*Regulatory Affairs Journals (File 183)

\*\*\*Index Chemicus (File 302)

\*\*\*Inspec (File 202)

RESUMED UPDATING

\*\*\*File 141, Reader's Guide Abstracts

\*\*\*

RELOADS COMPLETED

\*\*\*File 516, D&B--Dun's Market Identifiers

\*\*\*File 523, D&B European Dun's Market Identifiers

\*\*\*File 531, American Business Directory

\*\*\* MEDLINE has been reloaded with the 2006 MeSH (Files 154 & 155)

\*\*\* The 2005 reload of the CLAIMS files (Files 340, 341, 942)

is now available online.

\*\*\*

DATABASES REMOVED

\*\*\*File 196, FINDEX

\*\*\*File 468, Public Opinion Online (POLL)

Chemical Structure Searching now available in Prous Science Drug Data Report (F452), Prous Science Drugs of the Future (F453), IMS R&D Focus (F445/955), Pharmaprojects (F128/928), Beilstein Facts (F390), Derwent Chemistry Resource (F355) and Index Chemicus (File 302).

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File 1:ERIC 1966-2006/Apr (c) format only 2006 Dialog

Set Items Description

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Cost is in DialUnits

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Terminal set to DLINK

? b 5,34,155,71

19may06 10:39:41 User291213 Session D20.1

\$0.38 0.109 DialUnits File1

\$0.38 Estimated cost File1

\$0.08 TELNET

\$0.46 Estimated cost this search

\$0.46 Estimated total session cost 0.109 DialUnits

SYSTEM:OS - DIALOG OneSearch

File 5:Biosis Previews(R) 1969-2006/May W2

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File 155:MEDLINE(R) 1951-2006/May 23  
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File 71:ELSEVIER BIOBASE 1994-2006/May W2  
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Set	Items	Description
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? s anecortave		
S1	136	ANECORTAVE
? s gluco?		
>>>File 5 processing for GLUCO?		stopped at GLUCOSAMINYLMURAMYLDIPEPTIDE
>>>File 34 processing for GLUCO?		stopped at GLUCOSYLATIONS
>>>File 155 processing for GLUCO?		stopped at GLUCOSYLDISACCHARIDE
S2	877370	GLUCO?
? s s1 and s2		
	136	S1
	877370	S2
S3	9	S1 AND S2
? rd		
S4	6	RD (unique items)
? t s4/full/all		

4/9/1 (Item 1 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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0015710387 BIOSIS NO.: 200600055782  
Glucocorticoid receptor binding and anti-angiogenic/anti-vasopermeability effects of the synthetic steroid, 9-dehydro cortexolone acetate  
AUTHOR: Edelman J L (Reprint); Lutz D; Castro M R  
AUTHOR ADDRESS: Allergan Pharmaceut Inc, Biol Sci, Irvine, CA 92715 USA\*\*  
USA  
JOURNAL: IOVS 46 (Suppl. S): p3943 2005 2005  
CONFERENCE/MEETING: Annual Meeting of the  
Association-for-Research-in-Vision-and-Ophthalmology Ft Lauderdale, FL,  
USA May 01 -05, 2005; 20050501  
SPONSOR: Assoc Res Vis & Ophthalmol  
ISSN: 0146-0404  
DOCUMENT TYPE: Meeting; Meeting Poster  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: Purpose: To determine the glucocorticoid receptor binding affinity and anti-angiogenic/anti-vasopermeability activity of the anti-angiogenic synthetic steroid 9-dehydro cortexolone acetate ( **anecortave** acetate). Methods: 9-dehydro cortexolone acetate ( 4, 9( 11)-pregnadien-17, 21-diol-3, 20-dione acetate) and its deacetylated congener ( 9-dehydro cortexolone; **anecortave** ) were purchased from Steraloids, Inc. Glucocorticoid receptor ( GR) binding affinity was determined by displacement of 3H-dexamethasone in human HeLa S3 cells using 10 nM - 10 mu M **anecortave** or **anecortave** acetate. Corneal neovascularization was initiated by central cornea chemical cautery in rats, and the extent of new vessel growth was measured by intravascular FITC-dextran fluorescence on day 4. **Anecortave** acetate was administered topically three times daily in suspension ( 0.1% - 2.5%). Blood-retinal barrier breakdown was induced in rabbits by intravitreal injection of 500 ng VEGF-165, and retinal leakage was measured two days later by subjective scoring of fluorescein angiograms. In this rabbit model, 1 mg **anecortave** acetate or the glucocorticoid triamcinolone acetonide was injected into the vitreous in a sterile saline suspension. The GR

antagonist mifepristone ( 50 mg/kg/day) was administered by subcutaneous injection. Results: **Anecortave** and **anecortave** acetate bind to the GR with Ki values of 160 nM and 209 nM, respectively. In a rat model of corneal angiogenesis, **anecortave** acetate (up to 2.5% topically, t.i.d.) failed to inhibit new blood vessel growth. In the same study, 0.1% dexamethasone inhibited corneal angiogenesis by similar to 80%. In rabbits, intravitreal **anecortave** acetate ( 1 mg) inhibited VEGF-induced retinal leakage by 71%, and this inhibitory effect was significantly reversed by the GR antagonist mifepristone. In the same model, 1 mg triamcinolone acetonide completely blocked VEGF-induced vascular leakage for >1 month. These results in rabbits suggest that **anecortave** acetate ( or **anecortave** ) activates GR signaling, or alternatively, that **anecortave** acetate may be metabolized within the rabbit eye ( but not the rat eye) to an active **glucocorticoid** . Conclusions: The anti-angiogenic steroid **anecortave** acetate binds to the **glucocorticoid** receptor in vitro, and significantly inhibits VEGF-mediated retinal vascular leakage in vivo. Its in vivo activity may be due to the conversion of **anecortave** acetate to an active **glucocorticoid** within the rabbit eye.

REGISTRY NUMBERS: 76-25-5: triamcinolone acetonide; 84371-65-3: mifepristone

DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Sense Organs--Sensory Reception

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia; Leporidae--Lagomorpha, Mammalia, Vertebrata, Chordata, Animalia; Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: HeLa S3 cell line (Hominidae); rabbit (Leporidae); rat (Muridae)

ORGANISMS: PARTS ETC: eye--sensory system; vitreous--sensory system; blood-retinal barrier--nervous system, circulatory system; central cornea--sensory system

COMMON TAXONOMIC TERMS: Humans; Primates; Lagomorphs; Animals; Chordates; Mammals; Nonhuman Vertebrates; Nonhuman Mammals; Rodents; Vertebrates

DISEASES: corneal neovascularization--eye disease; retinal leakage--eye disease

MESH TERMS: Corneal Neovascularization (MeSH)

CHEMICALS & BIOCHEMICALS: **glucocorticoid** ; triamcinolone acetonide--antiinflammatory-drug; **glucocorticoid** receptor--binding; anti-angiogenic--topical administration; anti-vasopermeability; 9-dehydro cortexolone acetate {**anecortave** acetate}--ophthalmic-drug; VEGF-165--enzyme inhibitor-drug, intravitreal administration; mifepristone--hormone-drug, subcutaneous administration

MISCELLANEOUS TERMS: corneal angiogenesis; Meeting Poster

CONCEPT CODES:

00520 General biology - Symposia, transactions and proceedings

02506 Cytology - Animal

02508 Cytology - Human

10060 Biochemistry studies - General

10064 Biochemistry studies - Proteins, peptides and amino acids

10067 Biochemistry studies - Sterols and steroids

12512 Pathology - Therapy

14504 Cardiovascular system - Physiology and biochemistry

20004 Sense organs - Physiology and biochemistry

20006 Sense organs - Pathology

20504 Nervous system - Physiology and biochemistry

22005 Pharmacology - Clinical pharmacology

22012 Pharmacology - Connective tissue, bone and collagen-acting drugs

22016 Pharmacology - Endocrine

22031 Pharmacology - Sense organs, associated structures and functions  
BIOSYSTEMATIC CODES:  
86215 Hominidae  
86040 Leporidae  
86375 Muridae

4/9/2 (Item 2 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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0015607392 BIOSIS NO.: 200510301892

**Inhibition of VEGF-induced endothelial cell poliferation and  
differentiation by steroidal and non-steroidal COX inhibitors with  
variable COX-1/COX-2 selectivity**

AUTHOR: Yang R (Reprint); McCollum G W; Bingaman D P; Penn J S  
AUTHOR ADDRESS: Vanderbilt Univ, Nashville, TN USA\*\*USA  
JOURNAL: IOVS 45 (Suppl. 1): pU741 APR 2004 2004  
CONFERENCE/MEETING: Annual Meeting of the  
Association-for-Research-in-Vision-and-Ophthalmology Ft Lauderdale, FL,  
USA April 24 -29, 2004; 20040424  
SPONSOR: Assoc Res Vis & Ophthalmol  
ISSN: 0146-0404  
DOCUMENT TYPE: Meeting; Meeting Poster  
RECORD TYPE: Abstract  
LANGUAGE: English

**ABSTRACT:** Purpose: Endothelial cell proliferation and differentiation are critical components of angiogenesis. Inhibition of VEGF-induced bovine retinal microvascularendothelial cell (BRMEC) proliferation and tube formation (differentiation) in vitro was tested with the following series of steroidal and non-steroidal cyclooxygenase (COX) inhibitors with varied COX-1/COX-2 selectivity: the deaminated derivative of nepafenac, celecoxib, rofecoxib, diclofenac salt, ketorolac tromethamine salt, NS398, SC560 and dexamethasone. The PKC-beta inhibitor, LY333531, and the active metabolite of **anecortave** acetate were used as known active controls. Methods: BRMEC were grown on 96-well plates coated with fibronectin/hyaluronic acid. Growth medium was added for 2d followed by serum free medium overnight. Test medium containing 25 ng/ml VEGF, 0.1%DMSO and COX inhibitorat concentrations ranging from 0.01 to 10 mM was added for 24 hr. BRMEC proliferation was assayed using a modified MTT assay. For tube formation, BRMEC were grown on 6-well plates, within a Vitrogen 100 growth matrix sandwich and incubated in growth medium for 2d. The medium was replaced with 0.5% FBS plus 25 ng/ml VEGF with and without COX inhibitor and 0.1% DMSO. The mean tube length of each experimental group was digitally analyzed after 48hr in the experimental medium. Results: All test compounds except dexamethasone demonstrated inhibition of VEGF-induced BRMEC proliferation ranging from 42%-100%. The deaminated derivative of nepafenac, the active metabolite of **anecortave** acetate and celecoxib appeared to be the most potent. All test compounds showed inhibition oftube formation ranging from 28%-100%, with the deaminated derivative of nepafenac celecoxib rofecoxib, diclofenac and ketorolac being the most effective. Conclusions: Rofecoxib and celecoxib are COX-2 selective NSAIDs, while the nepafenac derivative and diclofenac are non-selective. Yet, the abilities of thesecompounds to inhibit endothelial cell proliferation and differentiation are comparable. Thus, it appears that COX selectivity is not a determining factor in the angiostatic activity demonstrated by these compounds.

REGISTRY NUMBERS: 169590-42-5: celecoxib; 50-02-2: dexamethasone;  
329900-75-6: cyclooxygenase-2; 9004-61-9: hyaluronic acid; 329967-85-3:

cyclooxygenase-1; 127464-60-2: VEGF; 162011-90-7: rofecoxib; 15307-86-5  
: diclofenac; 74103-07-4: ketorolac tromethamine; 123653-11-2: NS398;  
188817-13-2: SC560; 7753-60-8: **anecortave** acetate; 78281-72-8:  
nepafenac; 169939-94-0: LY333531

DESCRIPTORS:

MAJOR CONCEPTS: Pharmacology; Cardiovascular System--Transport and  
Circulation; Enzymology--Biochemistry and Molecular Biophysics; Sense  
Organs--Sensory Reception

BIOSYSTEMATIC NAMES: Bovidae--Artiodactyla, Mammalia, Vertebrata,  
Chordata, Animalia

ORGANISMS: BRMEC cell line (Bovidae)--bovine retinal microvascular  
endothelial cells

COMMON TAXONOMIC TERMS: Animals; Artiodactyls; Chordates; Mammals;  
Nonhuman Vertebrates; Nonhuman Mammals; Vertebrates

CHEMICALS & BIOCHEMICALS: celecoxib--enzyme inhibitor-drug; fibronectin  
; dexamethasone-- **glucocorticoid** -drug; cyclooxygenase-2 {COX-2};  
hyaluronic acid; cyclooxygenase-1 {COX-1}; VEGF {vascular endothelial  
growth factor}; rofecoxib--enzyme inhibitor-drug; diclofenac--enzyme  
inhibitor-drug; ketorolac tromethamine--enzyme inhibitor-drug; NS398--  
enzyme inhibitor-drug; SC560--enzyme inhibitor-drug; PKC-beta {protein  
kinase C-beta}; **anecortave** acetate; nepafenac--enzyme inhibitor-drug;  
LY333531--enzyme inhibitor-drug

MISCELLANEOUS TERMS: cell differentiation; cell proliferation; cell  
growth; Meeting Poster

CONCEPT CODES:

00520 General biology - Symposia, transactions and proceedings  
02506 Cytology - Animal  
10060 Biochemistry studies - General  
10064 Biochemistry studies - Proteins, peptides and amino acids  
10068 Biochemistry studies - Carbohydrates  
10802 Enzymes - General and comparative studies: coenzymes  
12512 Pathology - Therapy  
14504 Cardiovascular system - Physiology and biochemistry  
17002 Endocrine - General  
20004 Sense organs - Physiology and biochemistry  
22002 Pharmacology - General  
22016 Pharmacology - Endocrine

BIOSYSTEMATIC CODES:

85715 Bovidae

4/9/3 (Item 3 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0015607330 BIOSIS NO.: 200510301830

**Local delivery of anecortave acetate inhibits laser-induced choroidal  
neovascularization (CNV) in the mouse**

AUTHOR: Bingaman D P (Reprint); Liu C; Landers R A; Gu X

AUTHOR ADDRESS: Alcon Res Ltd, Retina Res, Ft Worth, TX USA\*\*USA

JOURNAL: IOVS 45 (Suppl. 1): pU730 APR 2004 2004

CONFERENCE/MEETING: Annual Meeting of the  
Association-for-Research-in-Vision-and-Ophthalmology Ft Lauderdale, FL,  
USA April 24 -29, 2004; 20040424

SPONSOR: Assoc Res Vis & Ophthalmol

ISSN: 0146-0404

DOCUMENT TYPE: Meeting; Meeting Poster

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Purpose: 1Anecortave acetate is an angiostatic cortisene devoid

of typical glucocorticoid activity that is undergoing phase III trials for the treatment of exudative AMD. Preclinically, **anecortave** acetate has been shown to reproducibly inhibit angiogenesis elicited by numerous stimuli in a variety of models, including preretinal neovascularization (NV). The following study assessed the utility of **anecortave** acetate in a commonly used posterior segment model, the mouse model of laser-induced choroidal NV. Method: Choroidal NV (CNV) was induced in C57BL/J mice by rupturing Bruch's membrane via focal laser photocoagulation. Each mouse received 3-4 laser burns per eye and was randomly assigned as noninjected controls, sham-injected controls, vehicle-injected eyes, or one of three **anecortave** acetate-injected groups. Control mice received laser OU, where one eye received a sham injection. For intravitreal-injected mice, one laser-treated eye received a 5 ul intravitreal injection of 0%, 0.1%, 1%, or 10% **anecortave** acetate. The pars plana intravitreal injection was performed immediately after laser photocoagulation. Fourteen days post-laser, all mice were euthanized and systemically perfused with fluorescein-labeled dextran. Eyes were then harvested and prepared as choroidal flat mounts, and CNV was quantified with computerized digital analysis. Mean CNV area per mouse was used for comparisons between treatment groups, where  $P < 0.05$  was considered significant. Results: An overall significant difference between treatment groups was established (Kruskal Wallis one-way ANOVA,  $P < 0.001$ ). Intravitreal injection of 10% **anecortave** acetate significantly prevented CNV development by 57.8% as compared to vehicle-injected eyes (Mann-Whitney Rank Sum test,  $P < 0.001$ ). No significant inhibition was observed in eyes treated with 0.1% or 1% **anecortave** acetate as compared to vehicle. Conclusions: **Anecortave** acetate provides significant inhibition of laser-induced choroidal neovascularization (CNV) when delivered locally in the adult mouse. These results support the robust package of preclinical efficacy pharmacology for **anecortave** acetate, thus, further substantiating its potential utility for treating pathologic ocular angiogenesis in man.

REGISTRY NUMBERS: 7753-60-8: **anecortave** acetate

DESCRIPTORS:

MAJOR CONCEPTS: Pharmacology; Cardiovascular System--Transport and Circulation; Sense Organs--Sensory Reception

BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: C57BL/J mouse (Muridae)--adult, animal model

ORGANISMS: PARTS ETC: eye--sensory system; pars plana--sensory system;

Bruch's membrane--sensory system; choroid--sensory system, angiogenesis

COMMON TAXONOMIC TERMS: Animals; Chordates; Mammals; Nonhuman Vertebrates; Nonhuman Mammals; Rodents; Vertebrates

DISEASES: choroidal neovascularization--vascular disease, eye disease, drug therapy, prevention and control, etiology; Bruch's membrane rupture--injury, eye disease, etiology

MESH TERMS: Choroidal Neovascularization (MeSH)

CHEMICALS & BIOCHEMICALS: **anecortave** acetate--ophthalmic-drug, pharmacodynamics, intravitreal administration, efficacy

METHODS & EQUIPMENT: laser photocoagulation--laboratory techniques, experimental surgical techniques; computerized digital analysis--mathematical and computer techniques

MISCELLANEOUS TERMS: ocular angiogenesis; Meeting Poster

CONCEPT CODES:

00520 General biology - Symposia, transactions and proceedings

12512 Pathology - Therapy

14504 Cardiovascular system - Physiology and biochemistry

14508 Cardiovascular system - Blood vessel pathology

20004 Sense organs - Physiology and biochemistry

20006 Sense organs - Pathology

22002 Pharmacology - General  
22031 Pharmacology - Sense organs, associated structures and functions  
BIOSYSTEMATIC CODES:  
86375 Muridae

4/9/4 (Item 4 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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0015246813 BIOSIS NO.: 200500153878  
**Safety of posterior juxtascleral depot administration of the angiostatic  
cortisene anecortave acetate for treatment of subfoveal choroidal  
neovascularization in patients with age-related macular degeneration**  
AUTHOR: Augustin Albert J (Reprint); D'Amico Donald J; Mieler William F;  
Schneebaum Cary; Beasley Cliff  
AUTHOR ADDRESS: Eye Clin, Stadt Klinikum Karlsruhe, Moltkestr 90, D-76133,  
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JOURNAL: Graefe's Archive for Clinical and Experimental Ophthalmology 243  
(1): p9-12 January 2005 2005  
MEDIUM: print  
ISSN: 0721-832X  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

**ABSTRACT:** Background: **Anecortave** acetate is a synthetic derivative of cortisol, but very specific and irreversible chemical modifications to the cortisol structure have resulted in the creation of a potent inhibitor of blood vessel growth with no evidence non-clinically or clinically of **glucocorticoid** receptor-mediated bioactivity. The clinical safety of **Anecortave** Acetate administered as a posterior juxtascleral depot every 6 months for up to 4 years is reviewed in this manuscript. Methods: Clinical safety and efficacy of the novel angiostatic agent **Anecortave** Acetate for Depot Suspension was evaluated in patients with subfoveal exudative age-related macular degeneration (AMD) in a masked, randomized, dose-duration clinical trial completed in June 2003. This safety and efficacy study enrolled and treated 128 patients at 18 clinical sites in the US and EU. This was the first clinical trial of **Anecortave** Acetate for Depot Suspension administered as a posterior juxtascleral depot. Assessments of clinical safety were made with general physical examinations including electrocardiograms and hematology/ serum chemistry/urinalysis, detailed ophthalmic evaluations with fluorescein/ indocyanine green angiography and assessments of best-corrected log-MAR visual acuity. All safety reports have been reviewed periodically by an Independent Safety Committee responsible for overseeing these activities. Results: No clinically relevant safety issues related to either **Anecortave** Acetate for Depot Suspension or the administration procedure have been identified by an Independent Safety Committee. The most frequent safety issues reported were cataractous changes, decreased visual acuity, ptosis, ocular pain, abnormal vision and subconjunctival hemorrhage, but the majority of these were assessed as unrelated to treatment. Conclusions: **Anecortave** Acetate for Depot Suspension ( 3, 15 and 30 mg) is clinically safe following administration and re-administration at 6-month intervals as a posterior juxtascleral depot using a specially designed curved cannula.

REGISTRY NUMBERS: 7753-60-8: **anecortave** acetate; 2321-07-5: fluorescein;  
3599-32-4: indocyanine green

DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Ophthalmology--  
Human Medicine, Medical Sciences; Pharmacology  
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata,  
Animalia  
ORGANISMS: human (Hominidae)  
COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates;  
Vertebrates  
DISEASES: macular degeneration--eye disease, diagnosis, drug therapy,  
symptom; subfoveal choroidal neovascularization--eye disease, diagnosis  
, drug therapy, symptom  
MESH TERMS: Macular Degeneration (MeSH); Choroidal Neovascularization  
(MeSH)  
CHEMICALS & BIOCHEMICALS: **anecortave** acetate--astringent-drug, dosage  
, efficacy, intraocular administration, juxtascleral depot  
administration, pharmacodynamics, safety; fluorescein;  
**glucocorticoid** receptor; indocyanine green  
METHODS & EQUIPMENT: angiography--clinical techniques, diagnostic  
techniques; electrocardiogram--clinical techniques, diagnostic  
techniques; urinalysis--clinical techniques, diagnostic techniques

CONCEPT CODES:

10060 Biochemistry studies - General  
10064 Biochemistry studies - Proteins, peptides and amino acids  
12504 Pathology - Diagnostic  
12512 Pathology - Therapy  
20006 Sense organs - Pathology  
22002 Pharmacology - General  
22005 Pharmacology - Clinical pharmacology

BIOSYSTEMATIC CODES:

86215 Hominidae

4/9/5 (Item 5 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0012530524 BIOSIS NO.: 200000248837

IOP lowering activity of **anecortave** acetate in rabbit and human  
glucocorticoid -induced ocular hypertension

AUTHOR: Clark A F (Reprint); DeFaller J (Reprint); Knepper P A; Robin A;  
Goode S M

AUTHOR ADDRESS: Alcon Research Ltd., Fort Worth, TX, USA\*\*USA

JOURNAL: IOVS 41 (4): pS511 March 15, 2000 2000

MEDIUM: print

CONFERENCE/MEETING: Annual Meeting of the Association in Vision and  
Ophthalmology. Fort Lauderdale, Florida, USA April 30-May 05, 2000;  
20000430

SPONSOR: Association for Research in Vision and Ophthalmology

DOCUMENT TYPE: Meeting; Meeting Abstract

RECORD TYPE: Citation

LANGUAGE: English

REGISTRY NUMBERS: 7753-60-8: **anecortave** acetate

DESCRIPTORS:

MAJOR CONCEPTS: Pharmacology; Sense Organs--Sensory Reception  
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata,  
Animalia; Leporidae--Lagomorpha, Mammalia, Vertebrata, Chordata,  
Animalia  
ORGANISMS: human (Hominidae); rabbit (Leporidae)--animal model  
COMMON TAXONOMIC TERMS: Humans; Primates; Animals; Chordates; Lagomorphs;  
Mammals; Nonhuman Vertebrates; Nonhuman Mammals; Vertebrates  
DISEASES: ocular hypertension--eye disease, **glucocorticoid** -induced



MESH TERMS: Ocular Hypertension (MeSH)

CHEMICALS & BIOCHEMICALS: **anecortave** acetate--intraocular pressure lowering activity

MISCELLANEOUS TERMS: intraocular pressure; Meeting Abstract; Meeting Abstract

CONCEPT CODES:

12512 Pathology - Therapy

20004 Sense organs - Physiology and biochemistry

20006 Sense organs - Pathology

22005 Pharmacology - Clinical pharmacology

00520 General biology - Symposia, transactions and proceedings

BIOSYSTEMATIC CODES:

86215 Hominidae

86040 Leporidae

4/9/6 (Item 1 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

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11346629 Genuine Article#: 641WB Number of References: 44

**Title: Anecortave acetate - Treatment of age-related macular degeneration angiogenesis inhibitor**

Author(s): Sorbera LA (REPRINT) ; Leeson PA; Castaner J; Bayes M

Corporate Source: Prous Sci,POB 540/Barcelona 08080//Spain/ (REPRINT);

Prous Sci,Barcelona 08080//Spain/

Journal: DRUGS OF THE FUTURE, 2002, V27, N11 (NOV), P1039-1048

ISSN: 0377-8282 Publication date: 20021100

Publisher: PROUS SCIENCE, SA, PO BOX 540, PROVENZA 388, 08025 BARCELONA, SPAIN

Language: English Document Type: ARTICLE

Geographic Location: Spain

Journal Subject Category: PHARMACOLOGY & PHARMACY

Abstract: Angiogenesis is a normal process that is strictly controlled. If this is strictly controlled. If this fine control is disrupted, chronic activation can occur resulting in inappropriate tissue responses that can lead to pathologic neovascularization. Many chronic ocular diseases are due to chronic stimulation of angiogenesis and they are they major cause of blindness worldwide. Treatment for these ocular neovascular disorders should involve delay, arrest or prevention of new capillary proliferation with the absence of or the presence of only minimal adverse events. To date, surgery, last photocoagulation and **glucocorticoid** therapy are the usual treatment options. However, they may be ineffective, worsen the condition or, in the case of **glucocorticoids**, be associated with steroid-induced adverse events. Several classes of antiangiogenic agents have been described and they include antibiotics, polypeptides, polycations, polyanions, steroids, VEGF antagonists and integrin antagonists. Angiostatic steroids in particular have been shown to inhibit angiogenesis without the typical steroid activity that is associated with side effects. One such novel angiostatic steroid chosen for further development is **anecortave** acetate. It has shown excellent preclinical antiangiogenic efficacy and promising clinical activity as a treatment for ocular neovascular disorders.

Identifiers--KeyWord Plus(R): ANGIOSTATIC STEROIDS; CORNEAL NEOVASCULARIZATION; INTEGRINS; RAT

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